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EXHIBIT A

SECOND SUPPLEMENTAL EXPERT REPORT

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1. This is my second supplemental expert report.

2. On December 8, 2011 the FDA convened a joint meeting of its Advisory Committees for Reproductive Health Drugs and its Drug Safety and Risk Management Committee [hereinafter "Joint Advisory Meeting"].

3. The agenda of the Joint Advisory Meeting involved issues relating to "the benefits and risks of drospirenone-containing oral contraceptives in light of the emerging safety concerns that the risk of venous thromboembolism (blood clots that can break lose [*sic*] and move with the circulatory system) associated with the use of these products may be higher compared to oral contraceptives that contain the progestin levonorgestrel. Drospirenone-containing oral contraceptives for the primary indication of pregnancy prevention include: Yasmin, Yaz (drospirenone/ethinyl estradiol tablets), Beyaz, Safyral (drospirenone/ethinyl estradiol/levomefolate calcium tablets and levomefolate calcium tablets), Bayer HealthCare, and the generic equivalents for these products." Transcript p. 4.

4. This was considered a "specific matters" meeting, also called a particular matters meeting, during which specific matters related to drospirenone-containing oral contraceptives was discussed. Transcript p. 4.

5. FDA uses advisory committees to provide expert advice and make recommendations to help the agency reach regulatory decisions, particularly concerning important issues surrounding the safety and efficacy of drugs, medical devices and biologics.

6. Under Federal law, this joint advisory committee was required to be in compliance with Federal ethics and conflict of interest laws. Transcript p. 3.

7. Members of Advisory Committees are Special Government Employees (SGEs).

8. In certain instances where there are certain conflicts of interest, waivers may be granted, accompanied by public disclosure.

9. According to the Chair of the Joint Advisory Committee, based on the agenda for the meeting and all financial interests reported by the committee members and temporary voting members, no conflict of interest waivers were issued in connection with the meeting. Transcript p. 4.

10. Among other statutory and regulatory requirements, federal regulations require the consideration of the appearance of a conflict of interest for advisory committee members who will be participating in a specific matters/parties meeting when "circumstances would cause a reasonable person with knowledge of the relevant facts to question [the member's] impartiality." 5 C.F.R. § 2635.502. [Emphasis added.]

11. I have reviewed documents available to me, including some confidential documents available to me that may not have been available to the Food and Drug Administration, that relate to potential conflicts of interest of members of the Joint Advisory Committee.

12. Based on my review of those documents, it is my opinion that certain members of the Advisory Committee did have conflicts of interest such that a reasonable person with knowledge of the relevant facts could question the member's impartiality.

13. The specific facts upon which I base my opinion are as follows:

Conflicts of Interest: Dr. Paula Hillard

14. In March 2003, Bayer's Barry Lee instructed that Bayer put a plan "in action to educate this Key Opinion Leader [Dr. Hillard]." That plan involved discussing VTE risk. BHCPYAZ009016414 [bracketed text added].

15. Dr. Paula Hillard in a 2008 document was considered by Bayer as a "Bayer trained speaker." BHCPYAZ029542811 at 817.

16. The same Bayer document states that Dr. Hillard was booked by Bayer for a "promotional program." *Id.*

17. A Bayer document listed Dr. Hillard as having YAZ Speaker Training in Dallas, Texas. BHCPYAZ024125313.

18. According to a 2008 a Bayer Corporate Account Update stated, "New west coast speaker…Paula Hillard, MD recently relocated from Cincinnati, OH to Stanford—this enables us to now have another huge Mirena and Yasmin advocate here in Nor Cal—she will be well utilized!" [Emphasis added] BHCPYAZ029390496 at 498.

19. A January 2, 2009 Bayer document states that Paula Hillard delivered lectures for Bayer for a "speaker program" BHCPYAZ02930509 at 511.

20. According to a June 22, 2009 e-mail by Bayer's Jeanette Planes, Dr. Hillard was a regional opinion leader who attended a "ROL working group to review YAZ CRM materials. BHCPYAZ030605364.

21. A June 25, 2009 e-mail by Tara McConathy, a senior project manager of MedPro communications, to Dr. Paula Hillard with a copy to Bayer's Jeanette Planes, stated "I have attached several documents for your review prior to the Working Group Teleconference this Friday." Included in those documents was a YAZ CRM Discussion Guide. BHCPYAZ024320332.

22. A July 22, 2009 e-mail from Bayer Carrie Murray confirmed that Dr. Paula Hillard was booked for taping on July 24 for a "HCP [Health Care Professional] Conversation." BHCPYAZ024070590.

23. A November 24, 2009 e-mail by Bayer's Jeanette Planes attaches a "proof of service" form "for the YAZ CRM video", by Paula Hillard. BHCPYAZ024223001.

24. A Bayer agreement request/transmittal form dated June 12, 2009, documented a request for consultation/service agreement with Dr. Paula Hillard in the amount of $1000 for participation in a working group to provide suggestions for the development of an HCP – only web portal and consumer slide, including what content and user tools are important to HCP's. Dr. Hillard was classified by Bayer as a Regional Thought Leader. According to the agreement request, Dr. Hillard was to be paid by a third-party vendor. BHCPYAZ019159547 – 550.

25. According to a Bayer Tactical Brief dated January 2010, "MedPro Communications, Inc. will organize a half day, 2-camera video shoot with Dr. Paula Hillard to illustrate patient counseling techniques on the safety of YAZ." BHCPYAZ019168387.

26. The same tactical brief stated, "Med Pro Communications, Inc. will work with a medical writer, Bayer's MLR team and Dr. Hillard to prepare a script for an 8-10 minute video clip. The counseling portion of the video (6-7 minutes) will show Dr. Hillard speaking on the phone with a patient who is currently on YAZ and has safety concerns that she would like to better understand." The key messages in the video were to "remind patients why they are on YAZ; ask if any problems have developed; review benefits and safety of YAZ; look at risks of all OCs; discuss potential problems with switching OCs." *Id.*

27. Dr. Hillard served as an advisor to Bayer at an October 16-17, 2010 meeting of a Bayer Scientific Advisory Board that advised the company on the benefits and limitations of post-marketing studies assessing the safety of pharmacologic agents in general, and the International Active Surveillance (INAS) model in particular. INAS is a study of safety of Yaz, including VTE risk. Key questions framing the discussion included "the strengths and limitations

of observational studies, if levongesterol continues to be the appropriate comparator, and if there are alternative approaches to safety study design that might generate data more quickly and with less confounders." BHCPYAZ032952917 at 921.

28. Dr. Hillard served as an advisor to Bayer at an October 16 – 17, 2010 meeting of Bayer's Women's Healthcare Scientific and Health Economics and Outcomes Research Advisory Board: YAZ Flex and Caddy. BHCPYAZ032952938.

29. A Bayer document discusses the preparation of an Advisory Board Agreement between Bayer and Dr. Hillard for 1.5 days of service in October 2010 for $6200. BHCPYAZ034336509.

30. A Bayer 2010 document under the heading "Adolescent Ad Board" 22 November 2010, Steigenberger Hotel, Berlin, under the subheading, "External Experts," listed Paula Hillard. BSPYAZ021224591 at 604.

31. On December 19, 2011 at 10:41 pm PST, I viewed a Stanford University Web page http://med.stanford.edu/profiles/frdActionServlet?choiceId=showCOIs&&fid=8093 that stated Dr. Hillard receives fees of $5,000 or more per year as a paid consultant for the following companies: Bayer Schering, Johnson & Johnson. According to the website the relationships have been reported with the companies listed below during the calendar year 2010.

Conflicts of Interest: Dr. Anne Burke

32. A footnote in a December 2008 manuscript titled "Effects of switching from oral transdermal or transvaginal contraception on markers of thrombosis" and published in the journal, *Contraception*, identified that Dr. Burke had a conflict of interest with regard to research funding from Berlex (Bayer).

33. A February 2008, manuscript titled "Multicenter Comparison of the Contraceptive Ring and Patch" published in the journal *Obstetrics & Gynecology* Vol. 111 stated that Dr. Burke has received research funding from Bayer Healthcare Pharmaceuticals.

34. A Bayer document listed Dr. Burke as a "Bayer Contraception Expert," and she was assigned a Bayer Contact. BHCPYAZ033557528-30. *See also* BHCPYAZ032980319.

Conflicts of Interest: Dr. Melissa Gilliam

35. A Bayer document labeled Women's Healthcare Opinion Management System shows a check in a box next to the term KOL [Key Opinion leader] Payment Made. Another box labeled, specify currency, was filled in with the phrase, "Dollars." The interaction date listed was June 9, 2009. Bayer made a KOL payment in Dollars. BSPYAZ002528290.

36. A Bayer 2010 document under the heading "Adolescent Ad Board" 22 November 2010, Steigenberger Hotel, Berlin, under the subheading, "External Experts," listed Dr. Melissa Gilliam. BSPYAZ021224501 at 604.

Conflicts of Interest: Dr. Julia V. Johnson

37. On December 20, 2011 at 12:43 am PST, I viewed a UMass Profile at http://profiles.umassmed.edu/profiles/ProfileDetails.aspx?From=SE&Person=1258 which listed four research projects of Julia Johnson with Bayer:

38. Bayer Pharmaceutical. "Multi-center, open-label, randomized study to assess the safety and contraceptive efficacy of two doses (in vitro 12 µg/24 h and 16 µg/24 h) of the ultra low dose levonorgestrel contraceptive intrauterine systems (LCS) for a maximum of 3 years in women 18 to 35 years of age." 10/07 - 11/08.

39. Bayer Pharmaceutical. "A multicenter, double-blind, randomized, placebo-controlled study to determine the lowest effective dose of oral Angeliq (drospirenone 0.5

mg/17ß-estradiol 0.5 mg, drospirenone 0.25 mg/17ß-estradiol 0.5 mg, and 17ß-estradiol 0.3 mg) for the relief of moderate to severe vasomotor symptoms in postmenopausal women over a treatment period of 12 weeks." 9/07- 8/08.

40. Berlex Pharmaceutical. "A Multicenter, randomized, open-label, parallel-group, active control study to evaluate the efficacy and safety of LNG IUS (Mirena) as compared to medroxyprogesterone acetate during 6 cycles of treatment in patients with idiopathic menorrhagia." 8/06-10/08.

41. Berlex Pharmaceutical. "A multicenter, double-blind, double-dummy, randomized, placebo-controlled study comparing a 2.2 mg 17ß-estradiol/0.69 mg levonorgestrel combination transdermal patch, and a 1 mg 17ß-estradiol transdermal patch with a placebo patch in postmenopausal women to determine the lowest effective dose of estradiol for the relief of moderate to severe hot flushes." 3/05-4/06.

42. This research includes work on drospirenone- containing hormonal products. Drospirenone-containing oral contraceptives were the subject of the December 8, 2011 Advisory Committee meeting.

Conclusion

43. Due to the complex dynamics that are part of FDA advisory committee meetings, and in light of the fact that a reasonable person with knowledge of the relevant facts could question the above members' impartiality, it is my opinion that the FDA advisory committee was not independent of Bayer, and its recommendations and votes need to be viewed as such.

44. Several new studies concerning the risk of drospirenone containing oral contraceptives have been reported since the date of my last report: an FDA phase I study, a study by Gronich, Lavi and Rennert published in the Canadian Medical Association, and a 2011 study

by Lidegaard published in the British Medical Journal. Nothing in these studies alter, and indeed they support, my opinion that Bayer had an obligation to inform the public when Bayer became aware of studies that demonstrated an increased risk to patients, but did not, in a timely manner, do so.

I hold the opinions expressed in this report to a reasonable degree of scientific and professional certainty.

I reserve the opportunity to revise this report based on new information.

Dated: December 2, 2011

David A. Kessler, M.D.

Documents reviewed by Dr. Kessler for Second Supplemental Report

Bates Stamped Material:

BHCPYAZ019268388
BHCPYAZ019170047
BHCPYAZ033557528
BHCPYAZ032980319
BHCPYAZ033737966
BHCPYAZ033345108
BHCPYAZ027714093
BSPYAZ020323471
BHCPYAZ008186317
BHCPYAZ008676250
BHCPYAZ024067197
BHCPYAZ022968939
BHCPYAZ019250663
BHCPYAZ024082369
BHCPYAZ032917013
BHCPYAZ016717038
BHCPYAZ019245675
BHCPYAZ017382638
BHCPYAZ016683426
BHCPYAZ007322584
BHCPYAZ009864771
BHCPYAZ008161471
BHCPYAZ010525294
BHCPYAZ031052916
BHCPYAZ019268438
BHCPYAZ008045644
BHCPYAZ028247072
BHCPYAZ022811321
BSPYAZ001871033
BHCPYAZ019249864
BSPYAZ020787403
BHCPYAZ032833749
BHCPYAZ024081952
BHCPYAZ009864733
BHCPYAZ024125749
BHCPYAZ034305097
BHCPYAZ023227923
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BHCPYAZ029390509
BHCPYAZ029390496
BHCPYAZ029542811
BHCPYAZ009016414

BHCPYAZ018121415
BHCPYAZ030605364
BHCPYAZ024070590
BHCPYAZ034642269
BHCPYAZ024223001
BHCPYAZ024320332
BHCPYAZ024070470
BHCPYAZ034345541
BHCPYAZ024096763
BHCPYAZ006061159
BHCPYAZ028835139
BHCPYAZ028833498
BHCPYAZ028876687
BHCPYAZ032840010
BHCPYAZ034670017
BHCPYAZ019215641
BHCPYAZ032960316
BHCPYAZ008130807
BHCPYAZ024125313
BHCPYAZ024078595
BSPYAZ002373243
BHCPYAZ019249868
BHCPYAZ019168387
BHCPYAZ024067216
BHCPYAZ024094482
BHCPYAZ008604345
BHCPYAZ019305151
BHCPYAZ009107845
BHCPYAZ019249854
BSPYAZ017119427
BSPYAZ001925499
BHCPYAZ019159547
BSPYAZ021224591
BHCPYAZ016450522
BHCPYAZ010711132
BHCPYAZ029171176
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BHCPYAZ024077377
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BHCPYAZ030196186
BHCPYAZ034760321
BHCPYAZ034651591
BHCPYAZ034650089
BHCPYAZ034728155
BHCPYAZ034653368
BHCPYAZ034673371
BHCPYAZ034655706
BHCPYAZ034733566
BHCPYAZ034824957
BHCPYAZ034760314
BSPYAZ021312927

Non-Bates Stamped Material:

Gronich, et al. "Higher risk of venous thrombosis associated with drospirenone-containing oral contraceptives: a population-based cohort study." *CMAJ*, 2011; DOI:10.1503/cmaj.110463

Lidegaard, et al., "Risk of venous thromboembolism from use of oral contraceptives, containing different progestogens and oestrogen doses: Danish cohort study,: 2001-9, *BMJ* 2011; 343:d6423doi:10.1136/bmj. d6423

Ouellett-Hellstrom/Sidney study of Combined Hormonal Contraceptives (CHCs), October 2011.

Transcript of December 8, 2011 Advisory Committee meeting

U.S. Code and Code of Federal Regulations, and FDA.gov website materials re Advisory Committees and Conflicts of Interest

All documents referenced in the Second Supplemental Report.